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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/355,793	09/21/1999	MARTIN BLASER	D5979	6942

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EXAMINER
PORTNER, VIRGINIA ALLEN

ART UNIT	PAPER NUMBER
1645	16

DATE MAILED: 07/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/355,793	Applicant(s) Blaser et al
	Examiner Portner	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 12, 2002*.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 5-13, and 15-18* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 5-13, and 15-18* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1, 5-13, and 15-18 are pending.

Claims 1,5-7, 9-13, 15-16 and 18 have been amended.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections Withdrawn

2. Claim 18 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, in light of the amendment of the claim to recite claim limitations that are clear.

3. Claim 1 rejected under 35 U.S.C. 112, second paragraph for reciting the phrase "wherein said strain is mutated to contain a DNA cassette encoding a" twice, has been obviated through claim amendment.

Claim 1 rejected under 35 U.S.C. 112, second paragraph for reciting a "wherein clause", in the future tense, is obviated through claim amendment.

Claim 5 rejected under 35 U.S.C. 112, second paragraph, in light of the amendment of claim 5 to recite the phrase "heterologous protein" which evidence original descriptive support in claim 1 from which claim 5 depends.

Claim 6 rejected under 35 U.S.C. 112, second paragraph, in light of the amendment of the claim to define which is inserted, is a coding sequence for a heterologous protein.

Claim 7 rejected under 35 U.S.C. 112, second paragraph, in light of the amendment of the claim to define the cassette to contain a 3' secretion signal and not binding region and does not contain a 5' LPS binding region.

Claim 8 rejected under 35 U.S.C. 112, second paragraph, in light the clarifying discussion provided on the record.

Claim 9 rejected under 35 U.S.C. 112, second paragraph, in light of the amendment of the claim to depend from claim 5 which defines the heterologous protein to be an immunogen.

Claim 10 rejected under 35 U.S.C. 112, second paragraph, in light of the amendment of the claim to insert the word --to-- before the word "occur".

Claim 12 rejected under 35 U.S.C. 112, second paragraph, in light of the amendment of the claim to define the phrase "recA mutant".

Claim 12 rejected under 35 U.S.C. 112, second paragraph, in light of the amendment of the claim to define that each strain only expresses one S-layer protein and a heterologous antigen.

Claim 12, rejected under 35 U.S.C. 112, second paragraph, in light of the amendment of the claim to define the mutation to eliminate expression of the RecA protein.

Claim 13 rejected under 35 U.S.C. 112, second paragraph, in light of the amendment of the claim to no longer recite the word "immunogen".

Claim 15 rejected under 35 U.S.C. 112, second paragraph, in light of the amendment of the claim to define the mutant strain of E.coli express sapC, sapD, sapE and sapF genes of C.fetus.

Claim 16 rejected under 35 U.S.C. 112, second paragraph, in light of the amendment of the claim to define the chimeric protein to encode a heterologous protein.

Claim 18 rejected under 35 U.S.C. 112, second paragraph, in light of the amendment of the claim to no longer recite the phrase "wherein all but one of the seven to nine sapA homologs are altered".

4. Claims 1, 5-9 rejected under 35 U.S.C. 103(a) as being unpatentable over of Blaser (1994 cited above.) in view of Lubitz et al (US pat. 5,470,573) in light of the heterologous antigen being inserted into the coding sequence for the outer membrane and comprises the S-layer protein, but is not inserted into the S-layer coding sequence as recited in amended claim 1.

Rejections Maintained

5. Claims 1, 5-9, 18 (amended claims) and 10-13, 15-17 (amended claims) are rejected under 35 U.S.C. § 112, first paragraph (Deposit), as applied to claims 10-13, 15-17, for the reasons set forth in the objection to the specification, for reasons of record in paper number 6 and arguments set forth below.

6. Claims 1, 6-8 are rejected under 35 U.S.C. 102(a) as being anticipated by Dworkin et al (March 1996) for reasons of record in paper number 6, arguments made of record in paper number 10 and arguments set forth below.

7. Claims 1, 6-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Blaser (November 1994)for reasons of record in paper number 6.

8. Claims 1, 5-13, 15-18 are rejected under 35 U.S.C. 112, first paragraph *(written description rejection)*, as previously applied to claims 15-18, in light of the amendment of the claims to recite the phrase "one or more" sapA homologs without any upper limit nor defined by a reference strain that comprises the plurality of sapA homolog coding sequences which read on SapCDEF, in additional to other sapA homolog coding sequences not described, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record in paper number 13, paragraph 30.

Response to Arguments

9. The rejection of Claims 1, 5-8, 18 and 10-13, 15-17 under 35 U.S.C. § 112, first paragraph (Deposit), as previously applied to claims 10-13, 15-17, is argued by stating that a mutant strain that contains a mutated recA gene will be deposited prior to allowance, and based upon this statement the rejection is requested to be held in abeyance.

10. It is the position of the examiner that the rejection was made for the lack of written description of the recA gene for Campylobacter fetus and the SapBCDE genes. The lack of

written description rejection is maintained in light of no perfected Deposit has been made of record.

It is also the position of the examiner that the instant specification does not describe the gene sequences of a plurality of sapA homologs present in any C.fetus stain, wherein claim 1 has been amended to recite the phrase "one or more" with no upper limited for the number of sapA homologs in the mutant strain, and the specific locations of all of the genes encompassed by all of the strains have not been described. While the instant specification utilized strain 23D(wild type) for analysis and teaches some conserved and unconserved peptide amino acid sequences from several strains at page 23, Example 23, but the instantly claimed invention is not limited to comprise the genetic material that encodes any of the recited peptide sequences, or refer to any specific reference strain for which the instant specification provide original descriptive support.

The claims are directed to genetically engineered mutant strains of C.fetus from any type strain, strain 23D is not being publicly available and has not been deposited to enable the claimed invention, and sapA homologs would read on sapA1, sapA2, sapB, sapC, sapD, sapE and sapF, all of which have not been described by a nucleotide sequence or reference strain.

Claim 1 should be amended to recite a deposited strain to enable the newly amended claim, as any name of a gene does not enable the nucleotide structure that encodes the corresponding protein, nor does a functional limitation of a protein without the corresponding gene structure enable the gene recited in all of the claims as the genus of genes represented by the recitation of the phrase "sapA homologs". The claimed invention has not been described in

sufficient terms that one of skill in the art would know that Applicant had possession of the claimed invention through describing a representative number of species. The rejection is maintained for reasons of record and for the reasons set forth above, in light of the claims having been amended to recite new claim limitations directed to a plurality of sapA homologs coding sequences that have been mutated, the nucleotides sequences of which have not been described.

11. Applicant argues the rejection of claims 1-2, 6-8 and 18 (amended) under 35 U.S.C. 102(a) as being anticipated by Dworkin et al (March 1996, Molecular Microbiology) by asserting that they do not have the paper by Dworkin et al and Blaser et al and could not respond to the examiner's arguments.

12. It is the position of the examiner that the Dworkin et al (March 1996, Molecular Microbiology) was cited and submitted in the instant Application in the International Search Report as the first appearing "Y" reference. Applicant through filing of a copy of the International search report, provided evidence that they had received a copy of the reference from the International Search Authority to which the instant Application claims priority.

It was also noted by the examiner that the Molecular Biology 1994, reference is co-authored by two of the inventors of the instantly claimed invention, specifically J. Dworkin and Martin J. Blaser. A courtesy copy of the reference is being provided here with. The rejection made of record is maintained.

13. Applicant's arguments filed with respect to Dworkin et al quoting the examiner's statement that "Dworkin et al teach mutant strains that have not been structurally mutated (see figure 3a,3b, 7 and Table 1)" have been considered.

14. While it is true the examiner made this argument, the statement contained a typographical error and should have read:

Dworkin et al teach mutant strains that have been both structurally mutated and not mutated (wild type strain).

The examiner's statement "Inherently the mutant strain of Dworkin anticipates the now claimed invention" was the rejection intended. The claimed genetically engineered mutant of C.fetus need not surface express the heterologous protein, but must express an altered sapA homolog on the surface, and Dworkin et al disclose 7 strains that have altered sapA homologs that had S-layer expression and serum sensitivity (see Figure 1, double cross over mutants, page 1242).

Dworkin et al also disclose a two open reading frames for sapA, specifically sapA and sap2A (see Figure 5 and narrative for figure), wherein sap2A comprised a heterologous coding sequence for a protein and expressed an altered Sap phenotype based upon the growth conditions of the strain (see Figure 6, drawings and narrative).

15. Applicant argues that the claims recite "the expression of said DNA cassette results in a S-layer protein that represents a chimera between the native S-layer protein and the heterologous protein encoded by the DNA cassette."

16. It is the position of the examiner that the claim limitations argued have been canceled by amendment by Applicant and are no longer recited in the claims. Applicant's arguments are not commensurate in scope with the instantly claimed invention.

17. Dworkin et al (March 1996) is argued to not teach or suggest insertion of a DNA cassette encoding a foreign heterologous protein alters a sapA homolog.

18. It is the position of the examiner that Dworkin et al at page 1250, Table 1, shows the various phenotypes which evidence altered Sap homolog expression, and at page 1247, Figure 6, the insertion of the kanamycin cassette into a sapA coding sequence is taught to result in the expression of a "truncated product" (narrative for Figure 6) which resulted in an altered SapA homolog protein containing strain. The reference does disclose, teach, suggest the insertion of a DNA cassette encoding a foreign heterologous protein results in the expression of an altered sapA homolog being surface expressed; the reference anticipates the instantly claimed invention.

19. The Dworkin et al reference is asserted not to teach away from the claimed invention through the loss of a cell surface S-layer.

20. It is the position of the examiner that Dworkin et al show a strain that comprised both sapA and sapA2 coding sequences, wherein the mutated strain was mutated through the insertion of the heterologous coding sequence into the sapA2 coding sequence resulted in a phenotype that evidenced expression of a truncated product (see Figure 6, narrative, page 1247 and Table 1, page 1250), and the other sapA coding sequence was expressed normally. The claimed invention does not require the surface expression of the heterologous protein, only the expression of "one or more altered sapA homologs on cell surface". A strain that normally would express both SapA2 and SapA, on the cell surface and is then mutated to only express SapA and a truncated SapA2 product, would result in an altered cell surface expression of SapA, due to the alteration of in the coding sequence of the sapA2 homolog, which is a sapA homolog.

The instantly claimed invention only requires the insertion of a heterologous coding sequence for a protein into the coding sequence of a sapA homolog and what portion of the mutated coding sequence is surface expressed in broadly claimed to be any portion of the sapA homolog and does not require the heterologous protein to be surface associated.

A sapA2 homolog that no longer expresses the encoded protein product, or only expresses a truncated product, but also comprises a fully expressed sapA gene, would evidence an altered sapA cell surface homolog because the sapA2 would only be partially, or no longer be surface expressed, resulting in the surface array components of the cell surface to be altered resulting in a new SapA phenotypic strain.

The claimed invention of amended claim 1 does not require the surface expression of the encoded heterologous protein. The claim only requires the insertion of the heterologous coding sequence into one or more of the sapA coding sequence, the resulting mutant strain evidencing an altered sapA phenotype, Dworkin et al discloses the embodiment now claimed.

21. The rejection of claims 1, 6-8 under 35 U.S.C. 102(b) as being anticipated by Blaser (November 1994) is argued by stating the examiner only provided an abstract of the document and states the disclosure of the abstract does not anticipate the instantly claimed invention.

22. It is the position of the examiner that the Blaser et al (Molecular Microbiology reference) was cited and submitted in the instant Application in the International Search Report as an "X" reference. Applicant through filing of a copy of the International search report, provided evidence that they had received a copy of the reference from the International Search Authority to which the instant Application claims priority.

It was also noted by the examiner that the Molecular Biology 1994, reference is co-authored by one of the inventors of the instantly claimed invention, specifically Martin J. Blaser. A courtesy copy of the reference is being provided here with. The rejection made of record is maintained.

23. The Blaser et al reference is asserted to not teach or suggest each and every aspect of the present invention.

24. It is the position of the examiner that the Blaser et al (1994, Mol. Microbiol.)reference does disclose mutant strains of C.fetus, wherein the mutant strains were produced through the insertion of a DNA cassette encoding a foreign heterologous protein into a coding sequence of a sapA homolog. The Blaser et al reference discloses that a truncated 50 kDa S-layer protein was surface expressed, although it was in minimal amounts (see page 456, col. 1, paragraph 2, sentence 2). In addition to the expression of the altered sapA homolog on the surface, expression of additional sapA coding sequences was found based upon the appearance of additional SapA protein bands on a immunoblot gel. (See page 456, col. 2, whole column; Figure 6, page 457, col. 1, top of page; see narrative at page 457, col. 2, first paragraph, entire narrative appearing at this location, and Figure 7, showing additional coding sequences; see page 458, col. 2, paragraph 1, the additional expression of a 127 kDa S-layer protein; see page 458, col. 2, Discussion section for allelic replacement defined for C.fetus). The reference discloses the instantly amended claimed invention and is maintained for reasons of record and arguments set forth herein.

25. The rejection of claims 1, 5-13, 15-18 under 35 U.S.C. 112, first paragraph, as previously applied to claims 15-17 (written description) is argued by stating that the rejection will be obviated through Deposit of a strain "which will be made".

26. It is the position of the examiner that the Deposit has not been made, so the rejection has not been obviated and therefore maintained.

27. The rejection of Claim 11 under 35 U.S.C. 112, second paragraph, is asserted to have been obviated by amending the claim to recite that the mutant bacteria contains "a chimeric protein comprising a heterologous antigen and a sapA homolog."

28. It is the position of the examiner that chimeric protein that comprises a heterologous antigen is still not distinctly claimed. The question "Has a plasmid been introduced into the strain" still has not been answered. What the source of the heterologous antigen is, is still not distinctly claimed. What is the coding sequence for the heterologous protein? The claim though it has been amended, is still not clear with respect to the various components of the mutant strain are.

Conclusion

29. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however,

will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

30.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp
July 17, 2002

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